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Synthesis, Characterization And Antimicrobial Activity of Pharmaceutically Important 1,2-Dihydroquinoline Derivatives

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ABSTRACT

In the present work, twelve novel dihydroquinoline derivatives were synthesized by acetylation, cyclisation and substitution reactions. Again a condensation reaction was carried out between primary amine (dihydroquinoline) and substituted aryl, alkyl sulphonyl chlorides, benzyl bromides and carboxylic acids. The structures of the synthesized compounds were characterized on the basis of IR, ^{1}H NMR, ^{13}C NMR and Mass spectral data. All synthesized compounds are screened for their antibacterial and anthelmintic activity. From the results it is concluded that, some of the compounds exhibited potent, rest of compounds exhibited mild to moderate antibacterial and anthelmintic activity.

Keywords: 3-Amino phenol, Acetic anhydride, Ethylacetoacetate, *o*-Phenylenediamine, Dihydro quinoline, Antibacterial activity, Anthelmintic activity.

INTRODUCTION

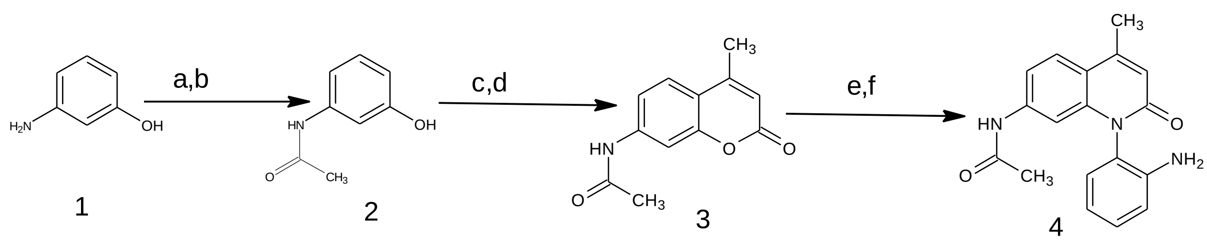
In continuation of our search of biologically important heterocyclic ring system [1, 2], the present study was undertaken. The chemistry of quinoline derivatives has been of increasing interest since many of these compounds have been found useful as chemotherapeutic agents against malarial parasite and microbes [3, 4]. It also reported that nitrogen and oxygen containing heterocyclics are one of the most extensively synthesized and screened compounds as they show diverse pharmacological properties including activity against microbes.

Quinolines constitute an important class of natural products belonging to the flavonoid family [5], which have been reported to possess a wide spectrum of biological activities, including anti-bacterial [6], anti-fungal [7], anti-inflammatory [8], anti-tumor [9], and anti-mutagenic [10]. Additionally, some of quinoline derivatives have been found to inhibit several important enzymes in cellular systems, such as xanthine oxidase [11], protein tyrosine kinase [12]. Hence, the synthesis of quinolines has generated vast interest among organic as well as medicinal chemist. Therefore we thought it worthwhile to synthesize quinoline derivatives and evaluate their antibacterial and anthelmintic activity.

MATERIALS AND METHODS

Melting points were determined in open capillary and are uncorrected. The structures of newly synthesized compound were established using IR, ^{1}H NMR, ^{13}C NMR and LC-MS data. FT-IR Spectra was recorded using Agilent Carry 630 FTIR with ATR instrument. ^{1}H NMR and ^{13}C NMR were recorded in Bruker model avance II (399.65 MHz, 1H NMR) and Bruker model avance II (100.50 MHz, 13C NMR) instruments respectively and analysis were carried out either DMSO-d_6 or CD_3OD depending on solubility of the compound. All the chemical shifts were reported in parts per million (ppm). LC-MS was recorded using Waters Alliance 2795 separations module and Waters Micromass LCT mass detector. Elemental analysis (C, H and N) was performed on an Elementar vario MICRO cube. The purity of the compound was confirmed using TLC on pre-coated silica gel plate and further purification was done using column chromatography.

Experimental: Synthetic route for preparation of 1,2-dihydroquinoline derivatives was shown in **scheme1**

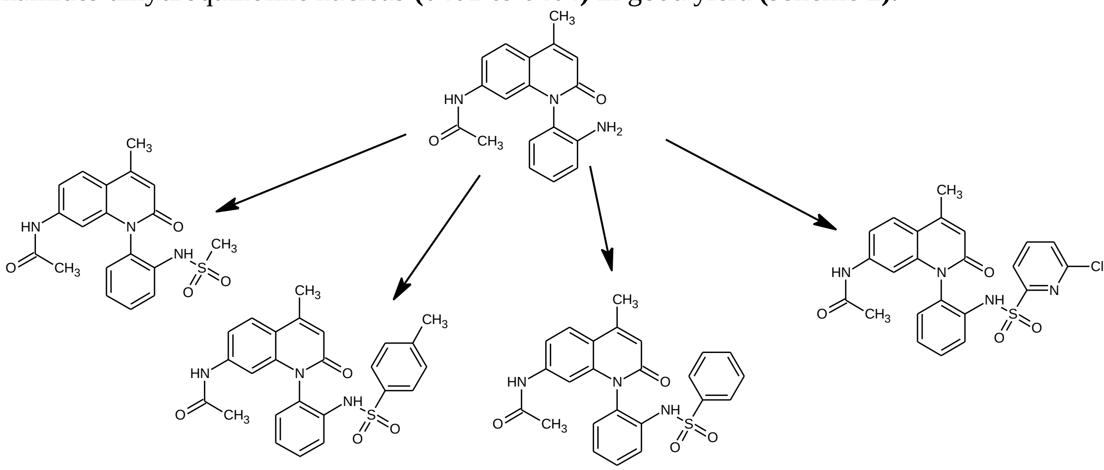


Procedure for the preparation of *N*-(3-hydroxyphenyl) acetamide (metacetamol) (2): Compound **(1)** (0.11 mol, 25g) was dissolved in acetic anhydride (a; 80 mL) and the reaction mixture was stirred at 60°C for 8 h at room temperature under nitrogen atmosphere. The excess acetic anhydride was removed under reduced pressure; the residue was dissolved in methylene dichloride (b; MDC), washed with water. The organic layer was separated, washed with brine, dried over Na_2SO_4 and concentrated to obtain compound **(2).** LCMS: 152 (M+1), m.p : 152 °C. Yield: 82%.

Procedure for the preparation of *N*-(4-methyl-2-oxo-2*H*-chromen-7-yl) acetamide (3): A mixture of 3-hydroxy acetanilide (metacetamol) (0.1 mol, 15.1g) and ethylacetoacetate (c; 0.1 mol) with 70% sulphuric acid (d, 50 mL) was heated carefully for 5 h. The resulting solution was cooled and poured over crushed ice (250 g). The crude product was filtered off and washed repeatedly with water, dried and recrystallized from hot water to result in title compound (**3).** LCMS: 205 (M+1), MP: 243 °C. Yield: 62%.

Procedure for the preparation of *N*-[1-(2-aminophenyl)-4-methyl-2-oxo-1,2-dihydroquinolin-7-yl]acetamide (4): A mixture of *N*-(4-methyl-2-oxo-2*H*-chromen-7-yl) acetamide (0.01 mol, 2.17g), o-phenylenediamine (e, 0.01 mol, 1.08g) and sodium acetate (f, 5 g) in glacial acetic acid (15 mL) was refluxed for 8 h and cooled [13,14]. The separated solid was filtered and recrystallized from methanol: water (1:2) to give title compound (**4).** LCMS : 237.8 (M+1), MP: 285 °C. Yield: 70%.

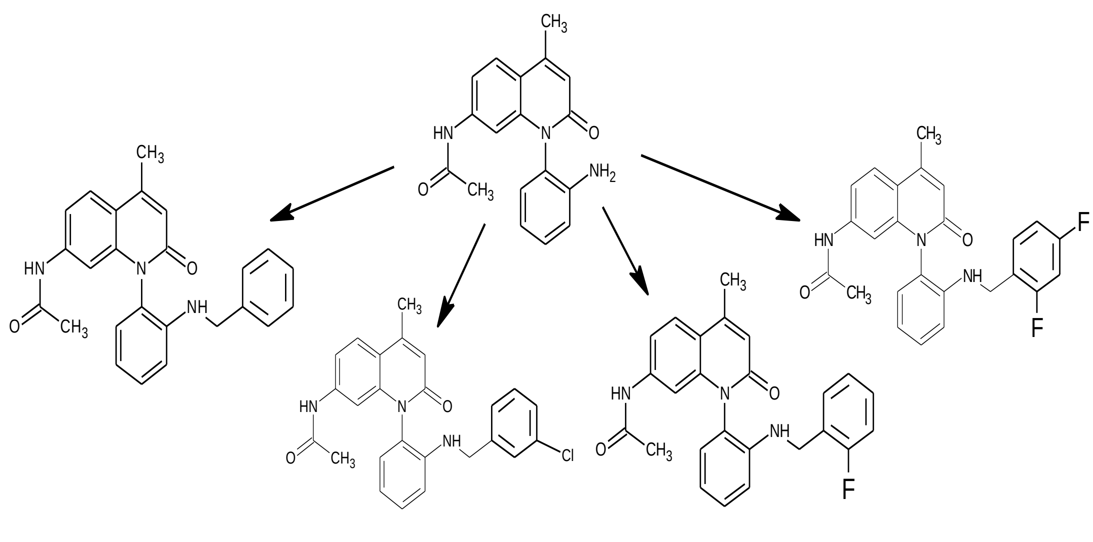
General Procedure for the preparation of sulphonamides containing dihydroquinoline nucleus (0401 to 0404): Equimolar quantities of compound (**4)** (0.001 mol, 0.5 g), and different substituted sulphonyl chlorides (0.001 mol) such as methyl-, p-tolyl-**,** phenyl- and 2-chloro pyridyl-sulfonyl chloride, and tetra ethyl amine (TEA, 0.003 moles, 0.57 g) were stirred in dry MDC (10 mL) under nitrogen condition at room temperature for 12 h. The reaction was monitored by TLC; mixture was washed with water and brine. The organic phase was dried over Na_2SO_4 and evaporated on vacuum. Residue was purified by column chromatography using petroleum ether:ethyl acetate as eluent (7:3) to get sulphonamides dihydroquinoline nucleus **(0401 to 0404)** in good yield **(scheme 2)**.



04 01 **04 02** **0403** **0404**

Scheme 2

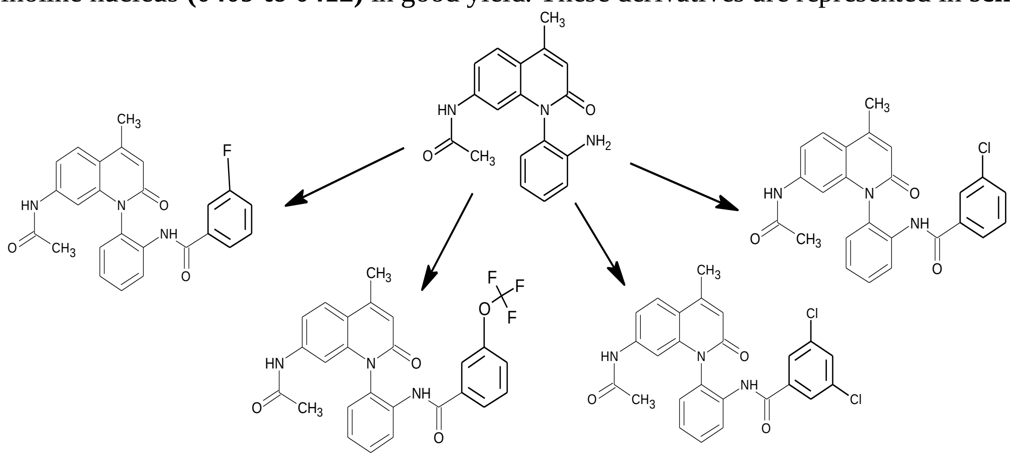
General Procedure for the preparation of benzylated dihydroquinoline nucleus (0405 to 0408): Equimolar quantities of compound **(4)** (0.5 g, 0.001 mol) and different substituted benzyl bromides (0.001 mol) such as benzyl-, 2-chloro benzyl-, 2-fluoro benzyl- and 2,4-difluoro benzyl bromides**,** K_2CO_3 (0.003 moles, 0.57 g), were stirred in dry ACN (10 mL) under nitrogen at room temperature for 10 h. The reaction was monitored by TLC and reaction mixture was filtered. The organic phase was dried over Na_2SO_4 and evaporated on vacuum. Residue was purified by column chromatography using petroleum ether: ethyl acetate as eluent (8:2) to get benzylated dihydroquinoline nucleus **(0405 to 0408)** in good yield **(scheme 3).**



0405 **0406** **0407** **0408**

Scheme 3

General Procedure for the preparation of amides containing dihydroquinoline nucleus (0409 to 0412): Equimolar quantities of compound (**4)** (0.001 mol, 0.5 g) and different substituted acid chlorides (0.001 mol) such as 3-fluoro benzoyl-**,** 3-trifluoromethoxy benzoyl-, 3,5-dichloro benzoyl- and 3-chloro benzoylchlorides, TEA (0.003 moles, 0.57 g), were stirred in dry MDC (10 mL) under nitrogen at room temperature for 10 h[14,15]. The reaction was monitored by TLC, reaction mixture was washed with water and brine. The organic phase was dried over Na_2SO_4 and evaporated on vacuum. Residue was purified by column chromatography using petroleum ether:ethyl acetate as eluent (7:3) to get amides containing dihydroquinoline nucleus **(0409 to 0412)** in good yield. These derivatives are represented in **scheme 4.**



0409 **0410** **0411** **0412**

Scheme 4

Antibacterial activity: The newly synthesized compounds were screened for their antibacterial activity. Concentrations of test compounds 400 µg/µl were prepared using DMSO and were tested against *S. Aureus, S. Citreus, B. Polymyx and B. Cereus* bacterial stains by disc diffusion method [16-17] using ciprofloxacin as standard (5 µg 50 μl^{-1}). The discs with 6.0 mm in diameter were prepared using filter paper. Discs were kept in screw capped bottle and sterilized at 140 ^oC for 1 h. Discs for the experiment were prepared by taking twice the amount of test compounds solution required for each disc was added to the bottle containing discs. Discs with different concentration of test compound were placed on the nutrient agar media in two sets on fresh bacteria seeded on agar media and incubated for 12 h at 35 ^oC. [18,19]

Determination of relative percentage inhibition: The relative percentage inhibition of the synthesized compounds with respect to positive control (Ciprofloxacin) was calculated by using the following formula [20].

$$\text{Relative Percentage inhibition} = \frac{100 \text{ x } (x - y)}{(z - y)}$$

Where, x= Total area of inhibition of the test extract, y= Total area of inhibition of the solvent
z= Total area of inhibition of the standard drug

Anthelmintic Activity: Anthelmintic activity of final compounds were done using *Pheretima posthuma* (Indian Earthworm), worms were maintained under normal vermicomposting medium with adequate supply of nourishment and water for about three weeks. Adult earthworms of approximately 4 cm in length and 0.2 - 0.3 cm in width were chosen for experiment [21,22]. Fourteen groups each with six earth worms were taken. Each *P. posthuma* was washed separately with normal saline before the initiation of experimental procedure and were placed into a 20 mL of normal saline. Group I earthworms were placed in 20 mL saline in a clean Petri plate and Group II earthworms were placed in 20 ml saline containing standard drug piperazine citrate (50 mg mL^{-1}). Similarly, Group III to XII earthworms were placed in a 20 mL saline containing 100 mg/mL of test samples. Observation was done keeping time taken for paralysis and the time taken for death as objective and was documented in minutes. Paralysis time was analyzed based on behavior of the worms with no revival body state in normal saline medium. Death was concluded based on total loss of motility with faded body color.

RESULTS AND DISCUSSION

In the present work, twelve novel dihydroquinoline derivatives were synthesized by acetylation of 3-amino phenol, cyclisation of N-(3-hydroxyphenyl) acetamidefollowed by substitution of o-phenylene diamine to get *N*-[1-(2-aminophenyl)-4-methyl-2-oxo-1,2-dihydroquinolin-7-yl]acetamide (4). Compound (4) was treated with various sulphonyl chlorides in order to get the dihydroquinoline derivatives with sulphonamide moiety (401 to 404); with benzyl bromides to obtain benzylated dihydroquinoline derivatives (405 to 408) and with different substituted acid chlorides to obtain amides containing dihydroquinoline derivatives (0409 to 0412). All the derivatives were obtained in good yield. Structures of synthesized compounds were elucidated based on IR, ^{1}H NMR, ^{13}C NMR and Mass spectra.

Spectral interpretation of final compounds

N-[1-(2-Methanesulfonylamino-phenyl)-4-methyl-2-oxo-1,2-dihydro-quinolin-7-yl]-acetamide, 0401: Yield: 82%; Melting point: 189-190 °C; MS: *m/z* = 385.44(M+1); IR: νmax/$cm^{-1:}$ 3340 (N-H), 2228 (CN), 1698 (CO), 1342–1140 (CF stretching); ^{1}H-NMR (DMSO-d_6) δ: 10.47 (s, 1H, NH), 7.88 (d, *J* = 8.7 Hz, 1H, Ar-H), 7.80 (d, *J* = 1.9 Hz, 1H, Ar-H), 7.45 (dd, *J* = 8.3 Hz and *J* = 1.5 Hz, 1H, Ar-H), 2.74 (t, *J* = 7.5 Hz, 2H, $COCH_2$), 2.67–2.55 (m, 2H, CF_3CH_2); ^{13}C-NMR (DMSO-d_6) δ: 169.3, 141.2, 138.3, 134.8, 128.7 CF_3, 125.9, 124.6, 115.9, 104.9, 28.7, 27.8; Elemental analysis: Calculated for:$C_{19}H_{19}N_3O_4S$; Calculated: C, 59.21 %; H, 4.97%; N, 10.90%; Observed: C, 59.19%; H, 4.95%; N, 10.84%.

N-{4-Methyl-2-oxo-1-[2-toluene-4-sulfonylamino)-phenyl]-4-methyl-2-oxo-1,2-dihydro-quinolin-7-yl}-acetamide, **0402:** Yield: 78%; Melting point: 212-214 °C; MS: *m/z* = 461.53 (M+1); IR: νmax/$cm^{-1:}$ 3340 (N-H), 2228 (CN), 1698 (CO), 1342–1140 (CF stretching); ^{1}H-NMR (DMSO-d_6) δ: 10.47 (s, 1H, NH), 7.88 (d, *J* = 8.7 Hz, 1H, Ar-H), 7.80 (d, *J* = 1.9 Hz, 1H, Ar-H), 7.45 (dd, *J* = 8.3 Hz and *J* = 1.5 Hz, 1H, Ar-H), 2.74 (t, *J* = 7.5 Hz, 2H, $COCH_2$), 2.67–2.55 (m, 2H, CF_3CH_2); ^{13}C-NMR (DMSO-d_6) δ: 169.3, 141.2, 138.3, 134.8, 128.7 CF_3, 125.9, 124.6, 115.9, 104.9, 28.7, 27.8; Elemental analysis: Calculated for:$C_{25}H_{23}N_3O_4S$; Calculated: C, 65.06 %; H, 5.02%; N, 9.10%; Observed: C, 65.05%; H, 5.00%; N, 9.09%.

N-[1-(2-benzenesulfonylamino-phenyl)-4-methyl-2-oxo-1,2-dihydro-quinolin-7-yl}-acetamide, 0403: Yield: 72%; Melting point 200-201 °C; MS: *m/z* = 447.51 (M+1); IR: νmax/$cm^{-1:}$ 3340 (N-H), 2228 (CN), 1698 (CO), 1342–1140 (CF stretching); ^{1}H-NMR (DMSO-*d6*) δ: 10.47 (s, 1H, NH), 7.88 (d, *J* = 8.7 Hz, 1H, Ar-H), 7.80 (d, *J* = 1.9 Hz, 1H, Ar-H), 7.45 (dd, *J* = 8.3 Hz and *J* = 1.5 Hz, 1H, Ar-H), 2.74 (t, *J* = 7.5 Hz, 2H, $COCH^2$), 2.67–2.55 (m, 2H, CF^3CH^2); ^{13}C-NMR (DMSO-d_6) δ: 169.3, 141.2, 138.3, 134.8, 128.7 CF^3, 125.9, 124.6, 115.9, 104.9, 28.7, 27.8; Elemental analysis: Calculated for:$C_{24}H_{21}N_3O_4S$; Calculated: C, 64.41 %; H, 4.73%; N, 9.39%; Observed: C, 69.39%; H, 4.71%; N, 9.35%.

N-{1-[2-(6-Chloro- pyridine-2-sulfonylamino)-phenyl]-4-methyl-2-oxo-1,2-dihydro-quinolin-7-yl}-acetamide, 0404: Yield: 72%; Melting point 181-182 °C; MS: *m/z* = 482.94 (M+1); IR: νmax/$cm^{-1:}$ 3340 (N-H), 2228 (CN), 1698 (CO), 1342–1140 (CF stretching); ^{1}H-NMR (DMSO-d_6) δ: 10.47 (s, 1H, NH), 7.88 (d, *J* = 8.7 Hz, 1H, Ar-H), 7.80 (d, *J* = 1.9 Hz, 1H, Ar-H), 7.45 (dd, *J* = 8.3 Hz and *J* = 1.5 Hz, 1H, Ar-H), 2.74 (t, *J* = 7.5 Hz, 2H, $COCH_2$), 2.67–2.55 (m, 2H, CF_3CH_2); ^{13}C-NMR (DMSO-*d6*) δ: 169.3, 141.2, 138.3, 134.8, 128.7 CF_3, 125.9, 124.6, 115.9, 104.9, 28.7, 27.8; Elemental analysis: Calculated for:$C_{23}H_{19}N_4O_4SCl$; Calculated: C, 57.20 %; H, 3.97%; N, 11.60%; Observed: C, 57.17%; H, 3.95%; N, 11.57%.

N-{1-(2- benzylamino-phenyl]-4-methyl-2-oxo-1,2-dihydro-quinolin-7-yl}-acetamide, 0405: Yield: 72%; Melting point 192-193 °C; MS: *m/z* = 397.47 (M+1).; IR: νmax/cm$^{-1:}$ 3340 (N-H), 2228 (CN), 1698 (CO), 1342–1140 (CF stretching); ^{1}H-NMR (DMSO-d_6) δ: 10.47 (s, 1H, NH), 7.88 (d, *J* = 8.7 Hz, 1H, Ar-H), 7.80 (d, *J* = 1.9 Hz, 1H; Ar-H), 7.45 (dd, *J* = 8.3 Hz and *J* = 1.5 Hz, 1H, Ar-H), 2.74 (t, *J* = 7.5 Hz, 2H, $COCH_2$), 2.67–2.55 (m, 2H, CF_3CH_2); ^{13}C-NMR (DMSO-d_6) δ: 169.3, 141.2, 138.3, 134.8, 128.7 CF_3, 125.9, 124.6, 115.9, 104.9, 28.7, 27.8; Elemental analysis: Calculated for:$C_{25}H_{23}N_3O_2$; Calculated: C, 75.54 %; H, 5.83%; N, 10.57%; Observed: C, 75.53%; H, 5.81%; N, 10.55%.

N-{1-[2-(3-Chloro-benzylamino)-phenyl]-4-methyl-2-oxo-1,2-dihydro-quinolin-7-yl}-acetamide, 0406: Yield: 72%; Melting point 199-200 °C; MS: *m/z* = 431.91 (M+1); IR: νmax/cm$^{-1:}$ 3340 (N-H), 2228 (CN), 1698 (CO), 1342–1140 (CF stretching); ^{1}H-NMR (DMSO-d_6) δ: 10.47 (s, 1H, NH), 7.88 (d, *J* = 8.7 Hz, 1H, Ar-H), 7.80 (d, *J* = 1.9 Hz, 1H, Ar-H), 7.45 (dd, *J* = 8.3 Hz and *J* = 1.5 Hz, 1H, Ar-H), 2.74 (t, *J* = 7.5 Hz, 2H, $COCH_2$), 2.67–2.55 (m, 2H, CF_3CH_2). ^{13}C-NMR (DMSO-d_6) δ: 169.3, 141.2, 138.3, 134.8, 128.7 CF_3, 125.9, 124.6, 115.9, 104.9, 28.7, 27.8. Elemental analysis: Calculated for:$C_{25}H_{22}N_3O_2Cl$; Calculated: C, 69.52 %; H, 5.13%; N, 9.73%.; Observed: C, 69.50%; H, 5.11%; N, 9.72%.

N-{1-[2-(3-Fluoro-benzylamino)-phenyl]-4-methyl-2-oxo-1, 2-dihydro-quinolin-7-yl}-acetamide, 0407: Yield: 72%; Melting point 212-214 °C; MS: *m/z* = 415.46 (M+1); IR: νmax/cm$^{-1:}$ 3340 (N-H), 2228 (CN), 1698 (CO), 1342–1140 (CF stretching). ^{1}H-NMR (DMSO-d_6) δ: 10.47 (s, 1H, NH), 7.88 (d, *J* = 8.7 Hz, 1H, Ar-H), 7.80 (d, *J* = 1.9 Hz, 1H, Ar-H), 7.45 (dd, *J* = 8.3 Hz and *J* = 1.5 Hz, 1H, Ar-H), 2.74 (t, *J* = 7.5 Hz, 2H, $COCH_2$), 2.67–2.55 (m, 2H, CF_3CH_2). ^{13}C-NMR (DMSO-d_6) δ: 169.3, 141.2, 138.3, 134.8, 128.7 CF_3, 125.9, 124.6, 115.9, 104.9, 28.7, 27.8. Elemental analysis: Calculated for:$C_{25}H_{22}N_3O_2F$; Calculated: C, 72.27 %; H, 5.34%; N, 10.11%. Observed: C, 72.25%; H, 5.31%; N, 10.08%.

N-{1-[2-(2,4-Difluro-benzylamino)-phenyl]-4-methyl-2-oxo-1,2-dihydro-quinolin-7-yl}-acetamide, 0408: Yield: 72%; Melting point 204-206 °C.; MS: *m/z* = 433.45(M+1). IR: νmax/cm$^{-1:}$ 3340 (N-H), 2228 (CN), 1698 (CO), 1342–1140 (CF streching). ^{1}H-NMR (DMSO-d_6) δ: 10.47 (s, 1H, NH), 7.88 (d, *J* = 8.7 Hz, 1H, Ar-H), 7.80 (d, *J* = 1.9 Hz, 1H, Ar-H), 7.45 (dd, *J* = 8.3 Hz and *J* = 1.5 Hz, 1H, Ar-H), 2.74 (t, *J* = 7.5 Hz, 2H, $COCH_2$), 2.67–2.55 (m, 2H, CF_3CH_2). ^{13}C-NMR (DMSO-d_6) δ: 169.3, 141.2, 138.3, 134.8, 128.7 CF_3, 125.9, 124.6, 115.9, 104.9, 28.7, 27.8. Elemental analysis: Calculated for: $C_{25}H_{21}N_3O_2F_2$ Calculated: C, 69.27 %; H, 4.88%; N, 9.69%. Observed: C, 69.25%; H, 4.86%; N, 9.65%.

N-[2-(7-Acetylamino -4 -methyl -2 oxo-2H-quinolin -1-yl)-phenyl]-3-fluoro-benzamide, 0409: Yield: 72%, Melting point : 221-223 °C. MS: *m/z* = 429.44 (M+1); IR: νmax/cm$^{-1:}$ 3340 (N-H), 2228 (CN), 1698 (CO), 1342–1140 (CF stretching); ^{1}H-NMR (DMSO-d_6) δ: 10.47 (s, 1H, NH), 7.88 (d, *J* = 8.7 Hz, 1H, Ar-H), 7.80 (d, *J* = 1.9 Hz, 1H, Ar-H), 7.45 (dd, *J* = 8.3 Hz and *J* = 1.5 Hz, 1H, Ar-H), 2.74 (t, *J* = 7.5 Hz, 2H, $COCH_2$), 2.67–2.55 (m, 2H, CF_3CH_2). ^{13}C-NMR (DMSO-d_6) δ: 169.3, 141.2, 138.3, 134.8, 128.7 CF_3, 125.9, 124.6, 115.9, 104.9, 28.7, 27.8. Elemental analysis: Calculated for: $C_{25}H_{20}N_3O_3F$; Calculated: C, 69.92 %; H, 4.69%; N, 9.78%. Observed: C, 69.90%; H, 4.66%; N, 9.76%.

N -[2-(7-Acetylamino -4 -methyl -2 oxo-2H-quinolin -1-yl)-phenyl]-3-methoxy-benzamide, 0410: Yield: 72%; Melting point 241-242 °C; MS: *m/z* = 495.44(M+1); IR: νmax/cm$^{-1:}$ 3340 (N-H), 2228 (CN), 1698 (CO), 1342–1140 (CF stretching). ^{1}H-NMR (DMSO-d_6) δ: 10.47 (s, 1H, NH), 7.88 (d, *J* = 8.7 Hz, 1H, Ar-H), 7.80 (d, *J* = 1.9 Hz, 1H, Ar-H), 7.45 (dd, *J* = 8.3 Hz and *J* = 1.5 Hz, 1H, Ar-H), 2.74 (t, *J* = 7.5 Hz, 2H, $COCH_2$), 2.67–2.55 (m, 2H, CF_3CH_2). ^{13}C-NMR (DMSO-d_6) δ: 169.3, 141.2, 138.3, 134.8, 128.7 CF_3, 125.9, 124.6, 115.9, 104.9, 28.7, 27.8. Elemental analysis: Calculated for:$C_{26}H_{20}N_3O_4F_3$; Calculated: C, 63.03 %; H, 4.07%; N, 8.48%. Observed: C, 63.02%; H, 4.04%; N, 8.44%.

N -[2-(7-Acetylamino -4 -methyl -2 oxo-2H-quinolin -1-yl)-phenyl]-3,5-dichloro-benzamide, 0411: Yield: 72%; Melting point 251-253 °C; MS: *m/z* = 480.34 (M+1); IR: νmax/cm$^{-1:}$ 3340 (N-H), 2228 (CN), 1698 (CO), 1342–1140 (CF streching); ^{1}H-NMR (DMSO-d_6) δ: 10.47 (s, 1H, NH), 7.88 (d, *J* = 8.7 Hz, 1H, Ar-H), 7.80 (d, *J* = 1.9 Hz, 1H, Ar-H), 7.45 (dd, *J* = 8.3 Hz and *J* = 1.5 Hz, 1H, Ar-H), 2.74 (t, *J* = 7.5 Hz, 2H, $COCH_2$), 2.67–2.55 (m, 2H, CF_3CH_2).^{13}C-NMR (DMSO-d_6) δ: 169.3, 141.2, 138.3, 134.8, 128.7 CF_3, 125.9, 124.6, 115.9, 104.9, 28.7, 27.8; Elemental analysis: Calculated for: $C_{25}H_{19}N_3O_3Cl_2$; Calculated: C, 62.51 %; H, 3.99%; N, 8.75%. Observed: C, 62.50%; H, 3.97%; N, 8.74%.

N -[2-(7-Acetylamino -4 -methyl -2 oxo-2H-quinolin -1-yl)-phenyl]-3-chloro-benzamide, 0412: Yield: 72%; Melting point: 218-219 °C; MS: *m/z* = 445.90 (M+1); IR: νmax/cm$^{-1:}$ 3340 (N-H), 2228 (CN), 1698 (CO), 1342–1140 (CF stretching); ^{1}H-NMR (DMSO-d_6) δ: 10.47 (s, 1H, NH), 7.88 (d, *J* = 8.7 Hz, 1H, Ar-H), 7.80 (d, *J* = 1.9 Hz, 1H, Ar-H), 7.45 (dd, *J* = 8.3 Hz and *J* = 1.5 Hz, 1H, Ar-H), 2.74 (t, *J* = 7.5 Hz, 2H, $COCH_2$), 2.67–2.55 (m, 2H, CF_3CH_2). ^{13}C-NMR (DMSO-d_6) δ: 169.3, 141.2, 138.3, 134.8, 128.7 CF_3, 125.9, 124.6, 115.9, 104.9, 28.7, 27.8. Elemental analysis: Calculated for:$C_{25}H_{20}N_3O_3Cl$; Calculated: C, 67.34 %; H, 4.52%; N, 9.42%. Observed: C, 67.32%; H, 4.49%; N, 9.39%.

Antibacterial activity: Antibacterial activity of tested compounds was carried out using disc diffusion method. It's suitability and working was ascertained by the use of ciprofloxacin. The standard drug exhibited higher zone of inhibition with all tested bacteria (24 to 28 mm). Out of all the synthesized compounds, 0402, 0404, 0408, 0410 and 0411 exhibited strong antibacterial activity against all the tested gram +ve bacteria as evident by higher relative percentage zone of inhibition (>80%). However, Compound 0402, 0408 and 0411 exhibited moderate activity against *S. aureus* (3.57%, 53.57% and 35.71% respectively). Remaining tested compounds showed lesser antibacterial activity. All the recorded zone of inhibition in mm and relative percentage inhibition values are tabulated in **Table 1**. Structure activity relationship studies reveal that 2-chloro pyridyl sulphonamide (0404), 2,4-difluoro benzyl (0408), 3-trifluoromethoxyl benzamide (0410) and 3,5-dichloro benzamide (0411) substituents were responsible for the observed effects.

Anthelmintic Activity: Anthelmintic activity of all the synthesised compounds were tested by treating with *Pheretima posthuma* (Indian Earthworm). Piperazine citrate is well known standard deworming drug. The paralysis time and death of worm was considered as marker of anthelmintic activity. Treatment of Piperazine citrate exhibited significant reduction ($p<0.01$) in both time taken for paralysis and death (39.17±0.48 & 57.00±0.58 respectively) when compared to saline treated group (142.33±0.49 & 167.17±0.87 respectively). Among tested compounds, 0402, 0407, 0409 and 0411 treatment showed significant ($p<0.01$) wormicidal in terms of paralysis and death of Indian earthworm. These four compounds exhibited comparable and even better activity than that of standard drug. Remaining eight compounds showed varied spectrum of activity **Table 2.** Pharmacophore such as p-tolyl sulphonamide (0402), 2-fluoro benzyl (0407), 3-fluoro benzamide (0409) and 3-chloro benzamide (0411) were responsible for the anthelmintic activity.

Table 1. Antibacterial activities of 1,2-dihyroquinoline derivatives

Compound	*S. Aureus*	*S. Citreus*	*B. polymyxa*	*B. cereus*
0401	02 (7.14)	16 (59.26)	18 (75.00)	19 (71.17)
0402	01 (3.57)	21 (77.78)	20 (83.33)	24 (100)
0403	04 (14.29)	08 (29.63)	10 (41.67)	12 (50.00)
0404	25 (89.29)	25 (92.59)	20 (83.33)	23 (95.83)

0405	04 (14.29)	06 (22.22)	06 (25.00)	08 (33.33)
0406	08 (28.57)	14 (51.85)	13 (54.17)	11 (45.83)
0407	11 (39.29)	17 (62.96)	NA	10 (41.67)
0408	15 (53.57)	26 (96.30)	22 (91.67)	21 (87.50)
0409	NA	17 (69.96)	12 (50.00)	10 (41.67)
0410	20 (71.43)	26 (96.30)	24 (100)	24 (100)
0411	10 (35.71)	16 (59.26)	18 (75.00)	20 (83.33)
0412	11 (39.29)	18 (66.67)	18 (75.00)	15 (62.50)
CIPX	28	27	24	24

Values in parentheses indicate relative percentage zone inhibition of test compounds compared to standard drug, Ciprofloxacin (CIPX). The zone of inhibition is expressed in mm.

Table 2. Anthelmintic activity of 1,2-dihydroquinoline derivatives

Test Samples	Concentrations (mg/ml)	Time taken for paralysis(min)	Time taken for death(min)
Control	_	142.33±0.49	167.17±0.87
Piperazine citrate	50	39.17±0.48**	57.00±0.58**
0401	100	56.00±2.28	68.50±0.41
0402	100	42.12±0.82**	56.17±0.60**
0403	100	62.50±0.76	81.67±0.71
0404	100	61.50±0.76	82.67±0.71
0405	100	48.33±1.22	54.00±0.59
0406	100	66.17±0.48	78.50±0.88
0407	100	28.32±1.45**	37.16±0.65**
0408	100	51.50±1.13	70.55±1.16
0409	100	30.545±1.12**	42.17±1.11**
0410	100	52.50±1.38	84.32±1.55
0411	100	26.00±2.18**	36.545±0.31**
0412	100	65.00±1.59	86.50±0.76

Values are the Mean±S.E.M of six earthworms (n=6). **p<0.01 compared control. One-way ANOVA followed by Dunnett post-test.

CONCLUSIONS

In the present research, some novel 1, 2 dihydroquinoline analogs were synthesized and were screened for their antimicrobial and anthelmintic activities. Compounds **0402, 0404, 0408, 041**, **0411** showed good activity against the tested bacteria with relatively higher percentage zone of inhibition. The compounds **0402, 0407, 0409 and 0411** possess significant anthelmintic activity. The observed activities may be due to the presence of sulphonamido, benzyl and amido moieties containing dihydroquinoline nucleus. Among 12 synthesized derivatives of novel 1, 2 dihydroquinoline, seven showed promising activity and possess active pharmacophore. Further studies are undergoing.

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